

WHAT IS CLAIMED IS:

- 1 1. A miniature fluidic system, comprising:
2 a body having at least two discrete reaction
3 chambers, each of said reaction chambers comprising at least
4 one vent port, and wherein each of said reaction chambers is
5 fluidly connected to a common chamber or channel;
6 a pneumatic system for selectively applying a
7 pressure differential between said common channel or chamber
8 and at least a selected one of said at least two discrete
9 chambers, whereby said pressure differential directs a fluid
10 sample in said body between said common channel or chamber and
11 said at least one selected chamber.
- 1 2. The system of claim 1, wherein said vent port
2 comprises a gas permeable fluid barrier disposed across said
3 vent port.
- 1 3. The system of claim 2, wherein said gas permeable
2 fluid barrier is a hydrophobic membrane.
- 1 4. The system of claim 1, wherein at least one of said
2 at least two chambers is a debubbling chamber, said debubbling
3 chamber comprising at least two vent ports, one of said at
4 least two vent ports being disposed at an intermediate
5 position in said chamber, whereby a bubble separating at least
6 two discrete fluid plugs in said chamber may exit said chamber
7 allowing said at least two discrete fluid plugs to connect.
- 1 5. The system of claim 1, further comprising a
2 controllable valve at the fluid connection between each of
3 said at least two discrete chambers and said common channel or
4 chamber.
- 1 6. The system of claim 5, wherein said controllable
2 valve is a diaphragm valve.

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1 7. The system of claim 81, wherein said pneumatic
2 system is further capable of applying a pressure differential
3 to said diaphragm valve to deflect said diaphragm valve.

1 8. The system of claim 7, wherein deflection of said
2 diaphragm valve opens said fluid connection.

1 9. The system of claim 1, wherein each of said chambers
2 has a cross sectional dimension of from about 0.05 to about 20
3 mm, and a depth dimension of from about 0.05 to about 5 mm.

1 10. The system of claim 1, wherein said at least two
2 chambers are fluidly connected via a fluid passage, said fluid
3 passage having a cross-sectional dimension of from about 10 μm
4 to about 1000 μm , and a depth dimension of from about 1 to 500
5 μm .

1 11. The system of claim 1, wherein said pneumatic system
2 comprises a pneumatic manifold for applying a differential
3 pressure between said at least first chamber and said at least
4 second chamber, to move said fluid sample from said at least
5 first chamber to said at least second chamber.

1 12. The system of claim 1, wherein said pneumatic system
2 comprises a differential pressure delivery system for
3 maintaining said at least first chamber at a first pressure
4 and said second chamber at a second pressure, said first
5 pressure being greater than ambient pressure and said second
6 pressure being greater than said first pressure, whereby when
7 said second chamber is brought to ambient pressure, said first
8 pressure forces a liquid sample in said first chamber into
9 said second chamber.

1 13. The system of claim 12 wherein said differential
2 pressure delivery system comprises:
3 a pressure source;

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4 at least first and second passages fluidly
5 connecting said pressure source to said at least first and
6 second chambers, respectively;

7 a first fluidic resistance disposed in said first
8 passage between said pressure source and said first chamber,
9 said first fluidic resistance transforming a pressure from
10 said pressure source to said first pressure;

11 a second fluidic resistance disposed in said second
12 passage between said pressure source and said second chamber,
13 said second fluidic resistance transforming said pressure from
14 said pressure source to said second pressure; and

15 first and second openable closures in said first and
16 second chambers, respectively, whereby opening of said first
17 or second closures allows said first or second chambers to
18 achieve ambient pressure.

1 14. The miniature system of claim 13, wherein said first
2 and second fluidic resistances independently comprise one or
3 more fluid passages connecting said first and second passages
4 to said first and second chambers, said first fluidic resistance
5 having a smaller cross-sectional area than said second fluidic
6 resistance.

1 15. The system of claim 1, wherein said pneumatic system
2 comprises a differential pressure delivery system for
3 maintaining said first chamber at a first pressure and said
4 second chamber at a second pressure, said second pressure
5 being less than ambient pressure and said first pressure being
6 less than said second pressure, whereby when said first
7 chamber is brought to ambient pressure, said second pressure
8 draws a liquid sample in said first chamber into said second
9 chamber.

1 16. The system of claim 15, wherein said differential
2 pressure delivery system comprises:
3 a pressure source;

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4 at least first and second passages fluidly
5 connecting said pressure source to said at least first and
6 second chambers, respectively;

7 a first fluidic resistance disposed in said first
8 passage between said pressure source and said first chamber,
9 said first fluidic resistance transforming a pressure from
10 said pressure source to said first pressure;

11 a second fluidic resistance disposed in said second
12 passage between said pressure source and said second chamber,
13 said second fluidic resistance transforming said pressure from
14 said pressure source to said second pressure; and

15 first and second openable closures in said first and
16 second chambers, respectively, whereby opening of said first
17 or second closures allows said first or second chambers to
18 achieve ambient pressure.

1 17. The system of claim 16, wherein said first and
2 second fluidic resistances independently comprise one or more
3 fluid passages connecting said first and second passages to
4 said first and second chambers, said first fluidic resistance
5 having a larger cross-sectional area than said second fluidic
6 resistance.

1 18. The system of claim 1, wherein said system further
2 includes a temperature controller disposed adjacent at least
3 one of said at least two chambers, for controlling a
4 temperature within said at least one chamber.

1 19. The system of claim 20, wherein said temperature
2 controller comprises a thermoelectric temperature controller.

1 20. The system of claim 20, wherein said temperature
2 controller comprises a resistive heater.

1 21. The system of claim 22, wherein said resistive
2 heating element is a NiCr/polyimide/copper laminate heating
3 element.

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1 22. The system of claim 20, further comprising a
2 temperature sensor disposed within said temperature controlled
3 chamber.

1 23. The system of claim 24, wherein said temperature
2 sensor is a thermocouple.

1 24. The system of claim 25, wherein said temperature
2 sensor is a resistance thermometer.

1 25. The system of claim 1, wherein at least one of said
2 at least two chambers is a cell lysis chamber and comprises a
3 cell lysis system disposed therein, for lysing cells in a
4 fluid sample.

1 26. The system of claim 25, wherein said cell lysis
2 system comprises an acoustic energy source disposed adjacent
3 said cell lysis chamber.

1 27. The system of claim 25, wherein said cell lysis
2 chamber includes microstructures fabricated on an internal
3 surface of said cell lysis chamber for enhancing cell lysis.

1 28. The system of claim 25, wherein said cell lysis
2 chamber includes an electrolytic pH control system for
3 altering a pH of said cell lysis chamber.

1 29. The system of claim 1, wherein at least one of said
2 at least two chambers is a hybridization chamber for analyzing
3 a component of a fluid sample, said hybridization chamber
4 including a polymer array, said polymer array including a
5 plurality of different polymer sequences coupled to a surface
6 of a single substrate, each of said plurality of different
7 polymer sequences being coupled to said surface in a
8 different, known location.

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1 30. The system of claim 29, wherein said polymer array
2 comprises at least 100 different polymer sequences coupled to
3 said surface of said single substrate, each of said plurality
4 of different polymer sequences being coupled to said surface
5 in a different, known location.

1 31. The system of claim 1, wherein said polymer array
2 comprises at least 1000 different polymer sequences coupled to
3 said surface of said single substrate, each of said plurality
4 of different polymer sequences being coupled to said surface
5 in a different, known location.

1 32. The system of claim 29, wherein said polymer array
2 comprises at least 10,000 different polymer sequences coupled
3 to said surface of said single substrate, each of said
4 plurality of different polymer sequences being coupled to said
5 surface in a different, known location.

1 33. The system of claim 1, wherein at least one of said
2 at least two chambers comprises a nucleic acid amplification
3 system.

1 34. The system of claim 33, wherein said nucleic acid
2 amplification includes a system for cycling a fluid sample in
3 said at least one chamber between at least two different
4 temperatures.

1 35. The system of claim 34, wherein said system for
2 cycling comprises at least two separate temperature controlled
3 chambers, said at least two chambers being maintained at at
4 least two different temperatures, whereby said sample is
5 cycled between said at least two temperatures by moving said
6 fluid sample back and forth between said at least two
7 temperature controlled chambers.

1 36. The system of claim 1, wherein at least one of said
2 at least two chambers comprises a nucleic acid purification

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3 system for separating nucleic acids in said sample from other
4 contaminants in said sample.

1 37. The system of claim 36, wherein said nucleic acid
2 purification system comprises a separation matrix for
3 separating said nucleic acids from said contaminants.

1 38. The system of claim 37, wherein said separation
2 matrix comprises functional groups for preferentially binding
3 said nucleic acids in said sample.

1 39. The system of claim 38, wherein said functional
2 groups comprise poly-T oligonucleotides.

1 40. The system of claim 37, wherein said nucleic acid
2 purification system further comprises an electrophoretic
3 system for applying an electric field to said fluid sample to
4 separate said nucleic acids from said contaminants.

1 41. The system of claim 37, wherein said separation
2 matrix comprises a gel matrix.

1 42. The system of claim 37, wherein said separation
2 matrix comprises a membrane disposed between said sample and
3 an anode of said electrophoretic system.

1 43. The system of claim 1, wherein at least one of said
2 at least two chambers is a reverse transcription chamber, said
3 reverse transcription chamber having disposed therein an
4 effective amount of a reverse transcriptase enzyme and the at
5 least four deoxynucleoside triphosphates.

1 44. The system of claim 1, wherein at least one of said
2 at least two chambers is an in vitro transcription chamber,
3 said in vitro transcription chamber having an effective amount
4 of an RNA polymerase and at least four different nucleoside
5 triphosphates, disposed therein.

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1 45. The system of claim 1, wherein at least one of said
2 at least two chambers comprises a nucleic acid fragmentation
3 system, for fragmenting a nucleic acid in a fluid sample.

1 46. The system of claim 45, wherein said fragmentation
2 system comprises a focused piezoelectric element disposed
3 adjacent said fragmentation chamber.

1 47. The system of claim 46, wherein said fragmentation
2 system further comprises a series of microstructures
3 fabricated on a first surface of said chamber.

1 48. The system of claim 45, wherein said fragmentation
2 system comprises at least one channel through which said fluid
3 sample is pumped, said channel having a submicron cross-
4 sectional dimension for generating a high-shear rate.

1 49. The system of claim 1, further comprising a fluid
2 mixing system for mixing said fluid sample within at least one
3 of said at least two chambers.

1 50. The system of claim 49, wherein said fluid mixing
2 system comprises a piezoelectric element disposed adjacent at
3 least one of said at least two chambers.

1 51. The system of claim 49, wherein said fluid mixing
2 system comprises a separate chamber adjacent to and fluidly
3 connected to said at least one of said at least two chambers,
4 whereby said fluid sample is flowed between said at least one
5 chamber and said separate chamber to mix said fluid sample.

1 52. The system of claim 49, wherein said mixing system
2 comprises:

3 a plurality of metallic particles disposed within
4 said at least one chamber;

5 an electromagnetic field generator adjacent said at
6 least one chamber, whereby when said electromagnetic field

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7 generator is activated, said metallic particles are vibrated
8 within said at least one chamber mixing contents of said
9 chamber.

1 53. The system of claim 49, wherein said mixing system
2 mixes a fluid sample contained in a hybridization chamber.

1 54. The system of claim 1, wherein said fluid transport
2 system comprises a micropump disposed in said body and fluidly
3 connected to at least one of said plurality of chambers.

1 55. The system of claim 54, wherein said micropump
2 comprises an electrophoretic pump.

1 56. A miniature fluidic system, comprising:
2 a body having at least first and second chambers
3 disposed therein, each of said at least first and second
4 chambers having a fluid inlet and being in fluid connection,
5 and at least one of said at least first and second chamber
6 being a hybridization chamber for analyzing a component of a
7 fluid sample, said hybridization chamber including a polymer
8 array, said polymer array including a plurality of different
9 polymer sequences coupled to a surface of a single substrate,
10 each of said plurality of different polymer sequences being
11 coupled to said surface in a different, known location;
12 a sample inlet, fluidly connected to at least one of
13 said first and second chambers, for introducing a fluid sample
14 into said system;
15 a fluid transport system for moving a fluid sample
16 from said at least first chamber to said at least second
17 chamber.

1 57. The system of claim 56, wherein said polymer array
2 comprises at least 100 different polymer sequences coupled to
3 said surface of said single substrate, each of said plurality
4 of different polymer sequences being coupled to said surface
5 in a different, known location.

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1 58. The system of claim 56, wherein said polymer array
2 comprises at least 1000 different polymer sequences coupled to
3 said surface of said single substrate, each of said plurality
4 of different polymer sequences being coupled to said surface
5 in a different, known location.

1 59. The system of claim 56, wherein said polymer array
2 comprises at least 10,000 different polymer sequences coupled
3 to said surface of said single substrate, each of said
4 plurality of different polymer sequences being coupled to said
5 surface in a different, known location.

1 60. The system of claim 56, wherein said body further
2 comprises a transparent region disposed over said
3 hybridization chamber for detecting hybridization of a
4 component of said fluid sample to said oligonucleotide array.

1 61. A miniature fluidic system, comprising:
2 a body having at least two distinct chambers
3 disposed therein, each of said at least two chambers being
4 fluidly connected to at least one other of said at least two
5 chambers;
6 a sample inlet, fluidly connected to at least one of
7 said at least two chambers, for introducing a fluid sample
8 into said at least one chamber;
9 a fluid transport system for moving a fluid sample
10 from at least a first chamber of said at least two chambers to
11 at least a second chamber of said at least two chambers; and
12 a separation channel for separating a component of
13 said fluid sample, said separation channel being fluidly
14 connected to at least one of said chambers and including at
15 least first and second electrodes in electrical contact with
16 opposite ends of said separation channel for applying a
17 voltage across said separation channel.

1 62. The system of claim 61, wherein at least one of said
2 at least two chambers is an extension reaction chamber, said

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3 extension reaction chamber being fluidly connected to said
4 separation channel, said extension reaction chamber having
5 disposed therein one or more reagents selected from the group
6 consisting of a DNA polymerase, deoxynucleoside triphosphates
7 and dideoxynucleoside triphosphates.

1 63. The system of claim 61, further comprising at least
2 four separation channels and at least four extension chambers,
3 each of said separation channels being fluidly connected to a
4 separate one of said at least four extension chambers, each of
5 said separate extension chambers having disposed therein a
6 different dideoxynucleoside triphosphate.

1 64. The system of claim 61, wherein said body further
2 comprises a transparent region disposed over said separation
3 channel for detecting said component of said fluid sample.

1 65. A miniature fluidic system, comprising:
2 a body having at least two chambers disposed
3 therein, at least one of said at least two chambers being an
4 in vitro transcription reaction chamber, said in vitro
5 transcription reaction chamber having an effective amount of
6 an RNA polymerase and four different nucleoside triphosphates,
7 disposed therein;
8 a sample inlet, fluidly connected to at least one of
9 said at least two chambers, for introducing a fluid sample
10 into said at least one chamber; and
11 a fluid transport system for moving a fluid sample
12 from at least a first of said at least two chambers to at
13 least a second chamber of said at least two chambers.

1 66. A miniature fluidic system, comprising:
2 a body having at least two chambers disposed
3 therein, at least one of said at least two chambers being a
4 cell lysis chamber, for lysing cells in said fluid sample,
5 said cell lysis chamber comprising a cell lysis system;

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6 a sample inlet, fluidly connected to at least one of
7 said at least two chambers, for introducing a fluid sample
8 into said at least one chamber; and
9 a fluid transport system for moving a fluid sample
10 from at least a first of said at least two chambers to at
11 least a second chamber of said at least two chambers.

1 67. The system of claim 66, wherein said cell lysis
2 system comprises a series of microstructures fabricated on an
3 internal surface of said lysis chamber, whereby flowing said
4 fluid sample over said microstructures results in lysis of
5 cells in said fluid sample.

1 68. The system of claim 67, wherein said cell lysis
2 system further comprises a piezoelectric element disposed
3 adjacent said cell lysis chamber for flowing said fluid sample
4 over said microstructures.

1 69. The system of claim 67, wherein said cell lysis
2 chamber comprises an electrolytic pH control system, for
3 altering a pH in said cell lysis chamber.

1 70. A miniature fluidic system, comprising:
2 a body having at least two chambers disposed
3 therein, at least one of said at least two chambers being a
4 nucleic acid purification chamber, for separating nucleic
5 acids in said fluid sample from other contaminants in said
6 fluid sample;
7 a sample inlet, fluidly connected to at least one of
8 said at least two chambers, for introducing a fluid sample
9 into said at least one chamber; and
10 a fluid transport system for moving said separated
11 nucleic acids from said nucleic acid chamber to said at least
12 a second chamber of said at least two chambers.

1 71. The system of claim 70, wherein said nucleic acid
2 purification system comprises a separation matrix which

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1 selectively binds nucleic acids in said fluid sample, but not
2 said other contaminants.

1 72. The system of claim 71, wherein said matrix
2 comprises a silica matrix.

1 73. The system of claim 72, wherein said silica matrix
2 comprises glass wool.

1 74. The system of claim 71, wherein said matrix
2 comprises a solid support having poly-T oligonucleotides
3 coupled to said solid support.

1 75. A miniature fluidic system, comprising:
2 a body having at least a first chamber fluidly
3 connected to a second chamber by a fluid passage;
4 a sample inlet, fluidly connected to said first
5 chamber, for introducing a fluid sample into said system;
6 a differential pressure delivery system for
7 maintaining said first chamber at a first pressure and said
8 second chamber at a second pressure, said first pressure being
9 greater than ambient pressure and said second pressure being
10 greater than said first pressure, whereby when said second
11 chamber is brought to ambient pressure, said first pressure
12 forces a liquid sample in said first chamber into said second
13 chamber.

1 76. The system of claim 75, wherein said differential
2 pressure delivery system comprises:
3 a pressure source;
4 at least first and second passages fluidly
5 connecting said pressure source to said at least first and
6 second chambers, respectively;
7 a first fluidic resistance disposed in said first
8 passage between said pressure source and said first chamber,
9 said first fluidic resistance transforming a pressure from
10 said pressure source to said first pressure;

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11 a second fluidic resistance disposed in said second
12 passage between said pressure source and said second chamber,
13 said second fluidic resistance transforming said pressure from
14 said pressure source to said second pressure; and

15 first and second openable closures in said first and
16 second chambers, respectively, whereby opening of said first
17 or second closures allows said first or second chambers to
18 achieve ambient pressure.

1 77. The system of claim 76, wherein said first and
2 second fluidic resistances independently comprise one or more
3 fluid passages connecting said first and second passages to
4 said first and second chambers, said first fluidic resistance
5 having a smaller cross-sectional area than said second fluidic
6 resistance.

1 78. The system of claim 76, wherein said first and
2 second fluidic resistances independently comprise one or more
3 fluid passages connecting said first and second passages to
4 said first and second chambers, said fluid passages of said
5 first fluidic resistance having a greater length than said
6 fluid passages of said second fluidic resistance.

1 79. A miniature fluidic system, comprising:

2 a body having at least a first chamber fluidly
3 connected to a second chamber;

4 a sample inlet, fluidly connected to said first
5 chamber, for introducing a fluid sample into said at first
6 chamber;

7 a differential pressure delivery source for
8 maintaining said first chamber at a first pressure and said
9 second chamber at a second pressure, said second pressure
10 being less than ambient pressure and said first pressure being
11 less than said second pressure, whereby when said first
12 chamber is brought to ambient pressure, said second pressure
13 draws a liquid sample in said first chamber into said second
14 chamber.

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1 80. The system of claim 79, wherein said at least a
2 first chamber is fluidly connected to said second chamber by a
3 fluid passage.

1 81. The system of claim 80, wherein said differential
2 pressure delivery system comprises:

3 a pressure source;

4 at least first and second passages fluidly
5 connecting said pressure source to said at least first and
6 second chambers, respectively;

7 a first fluidic resistance disposed in said first
8 passage between said pressure source and said first chamber,
9 said first fluidic resistance transforming a pressure from
10 said pressure source to said first pressure;

11 a second fluidic resistance disposed in said second
12 passage between said pressure source and said second chamber,
13 said second fluidic resistance transforming said pressure from
14 said pressure source to said second pressure; and

15 first and second openable closures in said first and
16 second chambers, respectively, whereby opening of said first
17 or second closures allows said first or second chambers to
18 achieve ambient pressure.

1 82. The system of claim 81, wherein said first and
2 second fluidic resistances independently comprise one or more
3 fluid passages connecting said first and second passages to
4 said first and second chambers, said first fluidic resistance
5 having a larger cross-sectional area than said second fluidic
6 resistance.

1 83. The system of claim 81, wherein said first and
2 second fluidic resistances independently comprise one or more
3 fluid passages connecting said first and second passages to
4 said first and second chambers, said first fluidic resistance
5 comprising passages having a shorter length than said channels
6 of said second fluidic resistance.

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1 84. A method of directing a fluid sample in a miniature
2 fluidic system, comprising:
3 providing a microfabricated device having at least
4 first and second chambers disposed therein, wherein each of
5 said at least first and second chambers is in fluid connection
6 with a common chamber or channel, has at least first and
7 second controllable valves disposed across said fluid
8 connection, respectively, and includes at least one vent;
9 applying a positive pressure to said common chamber
10 or channel;
11 selectively opening said at least first controllable
12 valve, whereby said positive pressure forces said fluid sample
13 from said common chamber or channel into said first chamber.

1 85. The method of claim 84, further comprising applying
2 a positive pressure to said at least first chamber and
3 selectively opening said at least first controllable valve,
4 whereby said positive pressure forces said fluid sample from
5 said at least first chamber into said common chamber or
6 channel.

1 86. The method of claim 85, wherein said vent comprises
2 a hydrophobic membrane sealably disposed across said vent,
3 whereby when said fluid sample contacts said hydrophobic
4 membrane, flowing of said fluid sample into said at least
5 first chamber stops.

1 87. The method of claim 84, wherein said at least first
2 and second controllable valves are selectively opened
3 pneumatically.

1 88. A method of mixing at least two discrete fluid
2 components in a microfabricated fluidic system, comprising:
3 providing a microfabricated channel having a vent
4 disposed at an intermediate location in said channel, said
5 vent having a gas permeable fluid barrier disposed across said
6 vent;

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7 introducing said at least two discrete fluid
8 components into said channel separated by a gas bubble;
9 flowing said at least two fluid components past said
10 vent, whereby said bubble exits said vent, allowing said at
11 least two fluid components to mix.

1 89. The method of claim 88, wherein said gas permeable
2 fluid barrier is a hydrophobic membrane.

Sub B1 90. A method of repeatedly measuring a known volume of a
2 fluid in a miniature fluidic system, comprising:
3 providing a microfabricated device having at least
4 first and second chambers disposed therein, wherein said at
5 least first and second chambers are in fluid connection, each
6 comprise at least one vent port, and wherein at least one of
7 said chambers is a volumetric chamber having a known volume;
8 filling said volumetric chamber with said fluid to
9 create a first aliquot of said fluid;
10 transporting said first aliquot of said fluid to
11 said at least second chamber; and
12 repeating said filling and transporting steps.

1 91. The method of claim 90, wherein each of said
2 chambers of said device provided in said providing step has a
3 cross sectional dimension of from about 0.05 to about 20 mm,
4 and a depth dimension of from about 0.05 to about 5 mm.

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